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FIG. 1a.

CYP3A5 Genotype/Phenotype Relationship

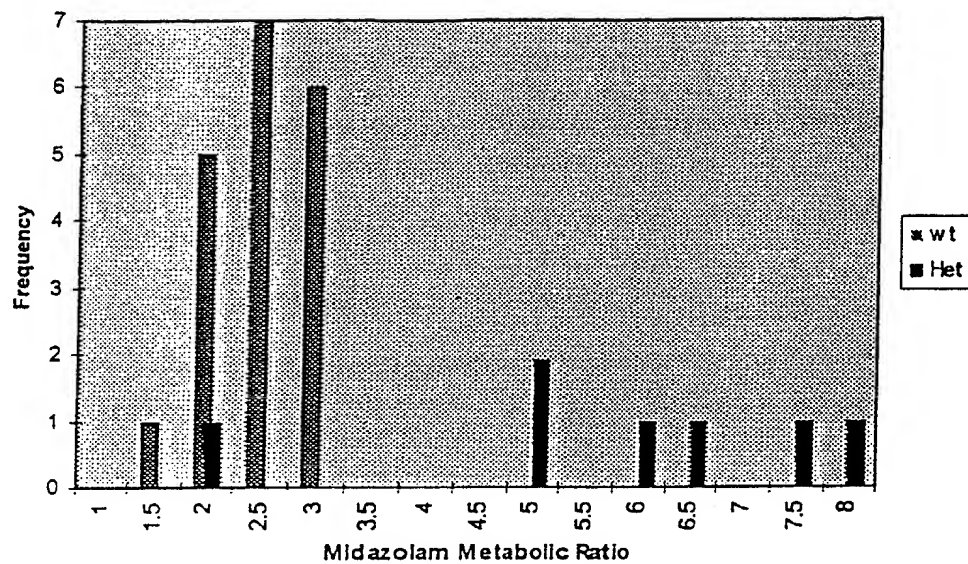


FIG. 1b.

CYP3A5 mRNA Expression Related to Genotype

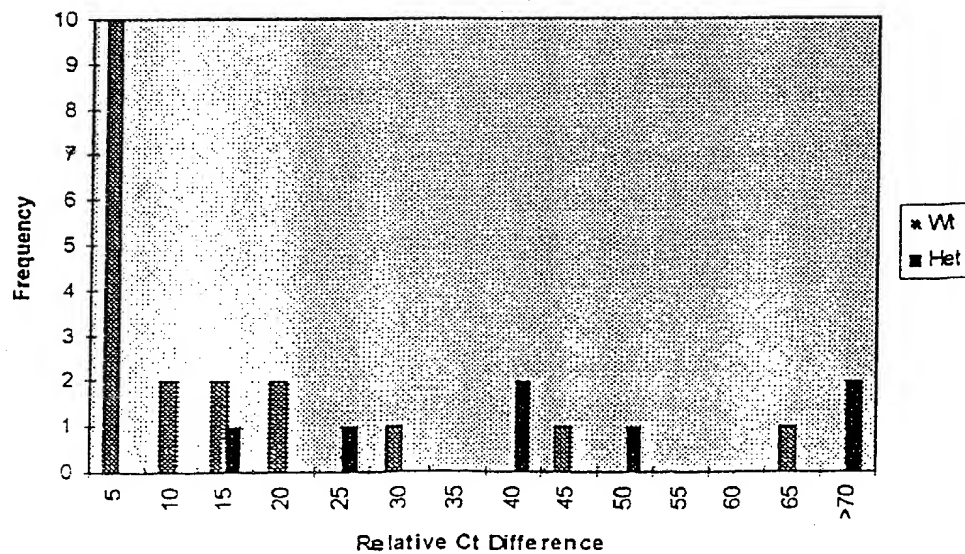
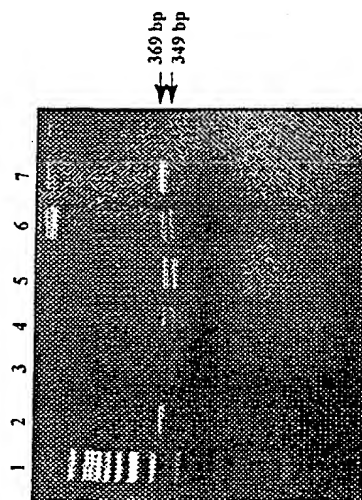
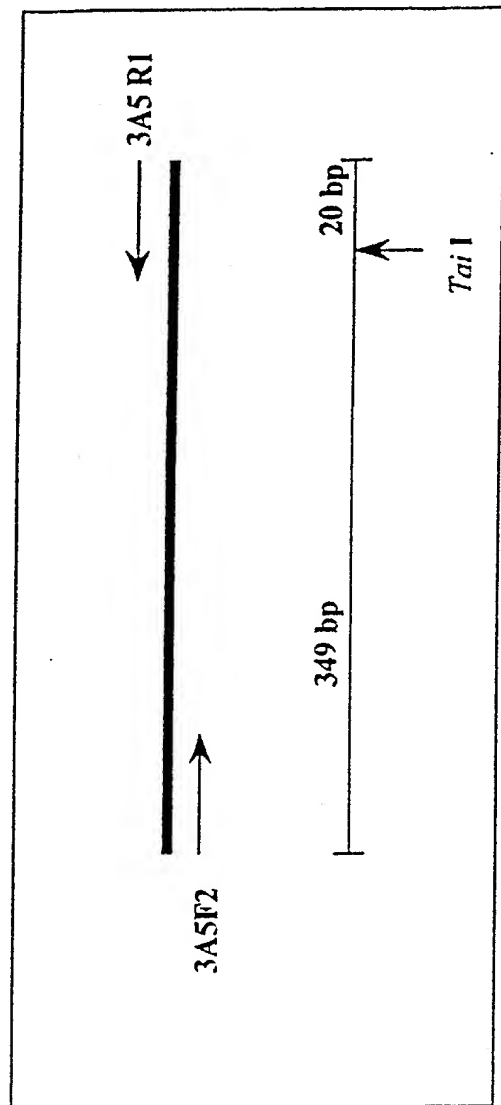


FIG. 2.



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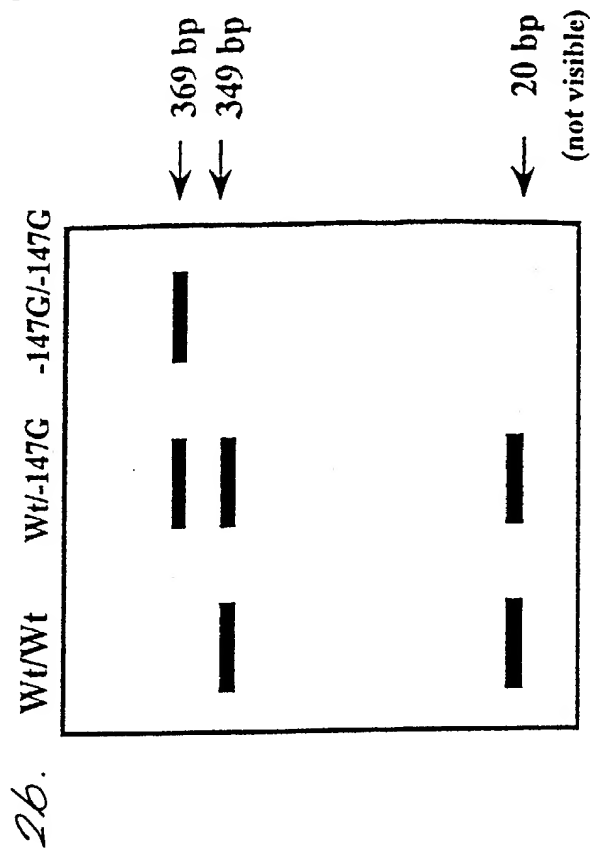
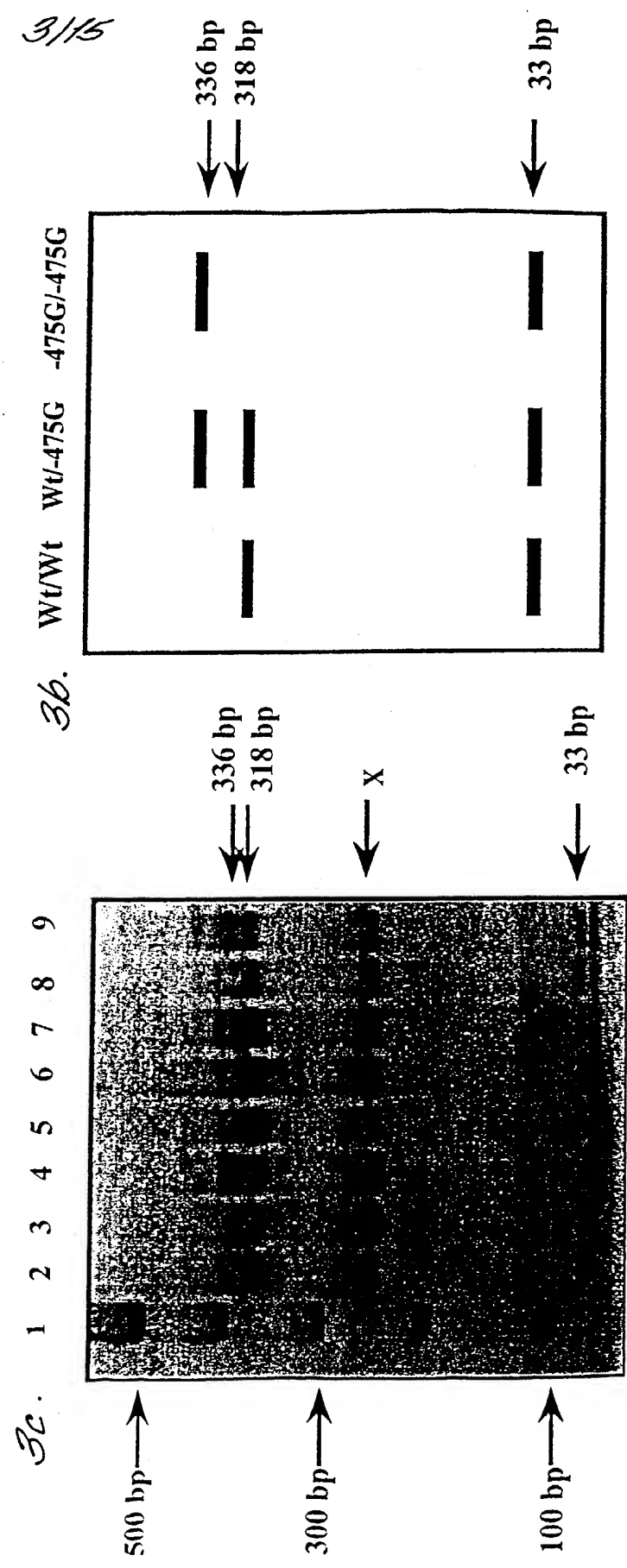
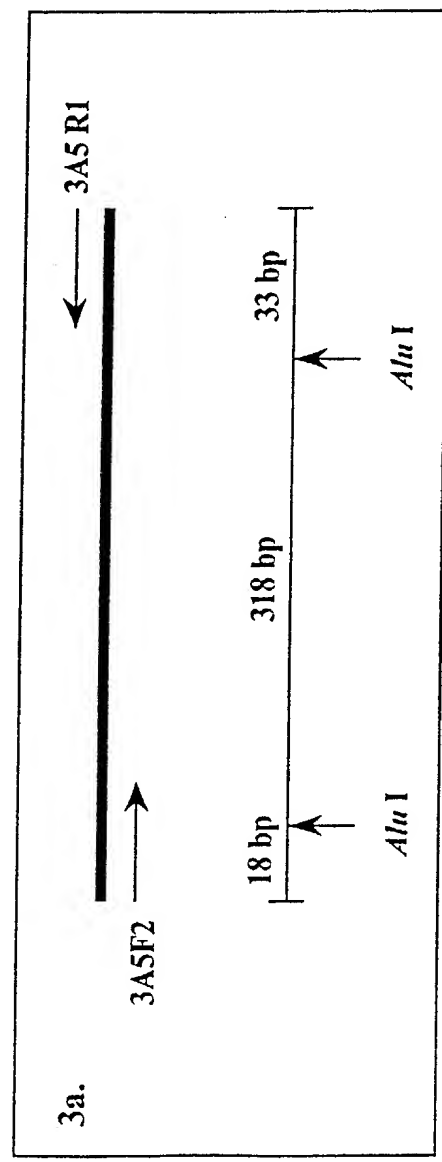


FIG. 3.



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FIG. 4a.

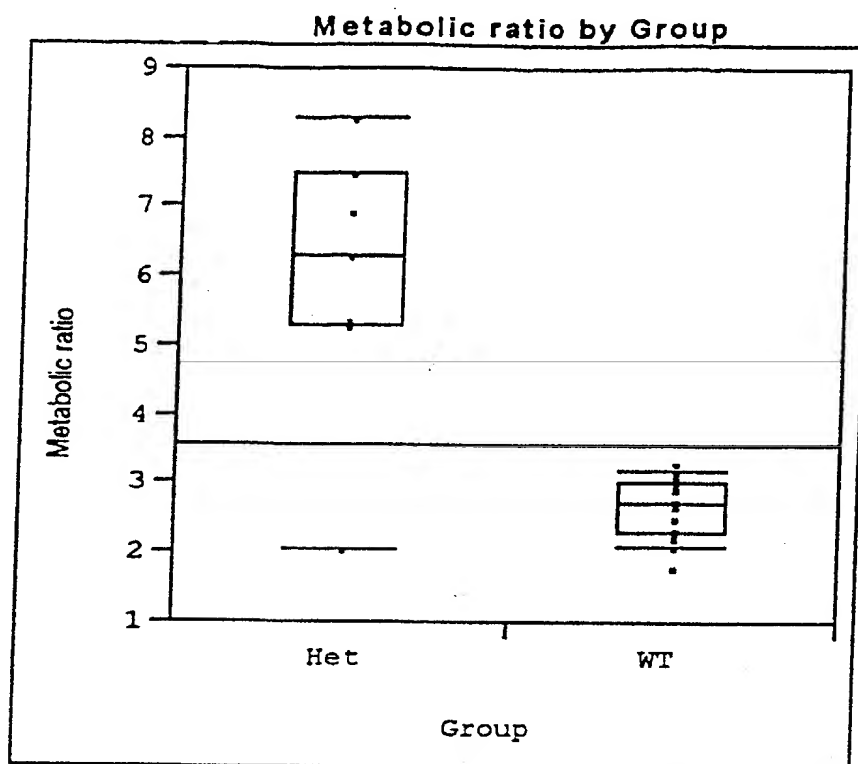
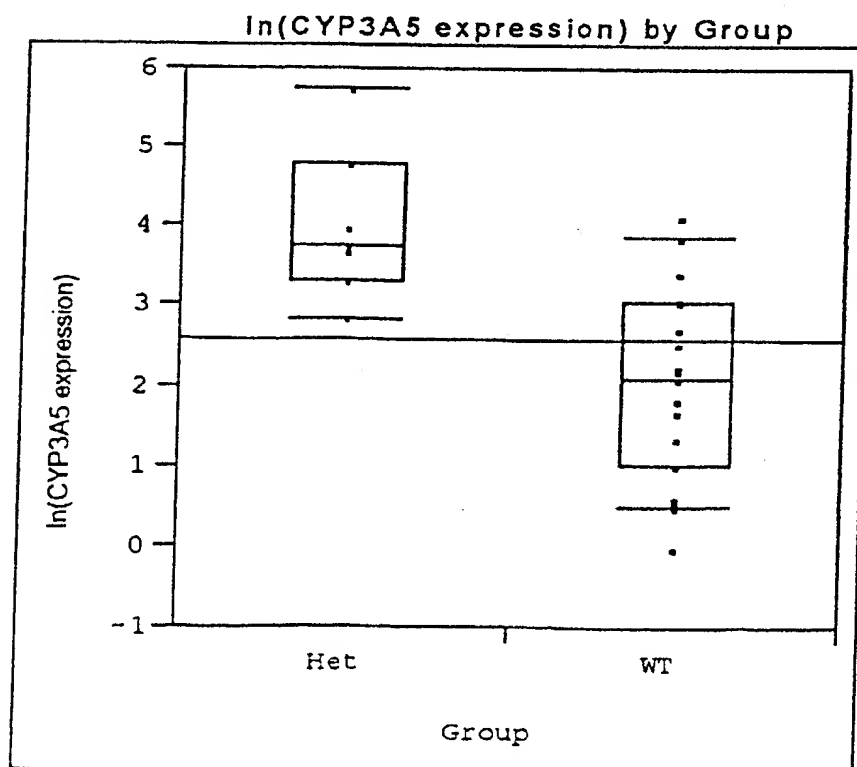
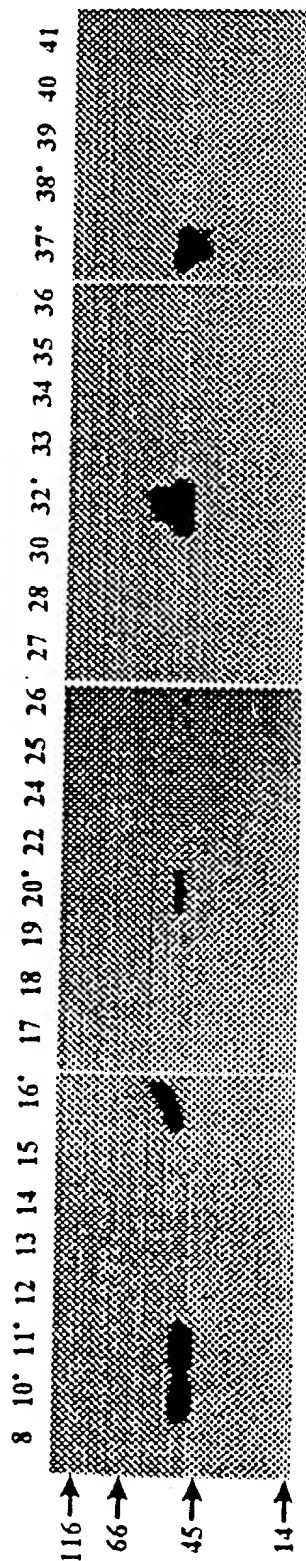


FIG. 4b.



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FIG. 5.



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FIG. 6.

3A5F1 5'-GGGTCTGTCTGGCTGCGC-3'

3A5F2 5'-GGGGTCTGTCTGGCTGAGC-3'

3A5R1 5'-TTTATGTGCTGGAGAAGGACG-3'

FIG. 7

-1343 GGAAGCAACC TACATGTCCA TCAACAGATG AATGGGTAAA GAGAGTACTT CACTTATGCA CAATGGAGTA
 -1273 CAATTCAGCC ATGAAAAAAG CATGAGATCC TGTCTTTTAT AATAACGTGG CTGGAACCTGC AGGTCATTAT
 -1203 GTTAGGTAAA ATAAGCCAGG CACACAAAGA CAGACATTGC ATGTTCTCAC TTATTTGTGG GATCTACAAA
 -1133 TCAAAACAAT TGAGCTAATG TCTGGGTCTT AGTCAATTTT GTACCCTAAG TACAGGGGAGC ACAGCCATTA
 -1063 GAATACATGA TGAATGCTTT AATACAGGAA TGAATAGGTG AGAGGCACAG GGTGGTTGGG TGTCTTCTG
 -993 ATACATAGTA TCTTCCTTGA CACATTCAGT ACAACTCTCA ACAGGTAAGT CTCTTCATGT ATGTTACCTT
 -923 CTGAGGAATT AAGTGGCAGA ACATGCCCTTC TATTATTTTC CTTGCAGAA CAAGACCAAT TGCATTAGTT
 -853 GGGAAACAGT GCTGGCTGCA TCTGAGCCCC AAGCAACCAT TAGTCTATTG CTATCACCAC AGACTCAGAG
 -783 GGGATGACAC ACAGGGGCCC AGCAATCTCA CCCAAGTCAA CTCCACCAAC ATTTCTGGTC ACCCACCATG
 -713 TGTACAGTAC CCTGCTAGGG TCCAGGGTCA TGAAAGTAAA TAATACCAGA CTGTGCCCTT GAGGAACCTCA
 -643 CCTCTGCTAA GGGAAACAGG CACAGAAACC CACAAGGGTG GTAGAGAGGA AATAGGACAA TAGGACTGTG
 -573 TGAGGGGGAT AGGAGGCACC CAGAGGAGGA AATGGTTACA TCTGTGTGAG GAGGTTGGTA AGGAAAGACT
 -503 TTAATAGAAG GGGTCTGTCT GGCTGGGCTT GCAAGGATGT GTAGGAGTCA TCTAGGGGGC ACAAGTACAC
 -433 TCCAGGCAGA GGAATTGCA TGGGTAAAGA TCTGCAGTTG TGGCTTGTGG GGATGGATTT CAAGTATTCT
 -363 GGAATGAAGA CAGCCATGGA AACAAGGGCA GGTGAGAGGA TATTAAAGAG GCTTCATGCC AATGGCTCCA
 -293 CTTCAGTTTC TGATAAGAAC TCAGGTTCCG TGGACTCCCT GATAAACTG ATTAAGTGT TTATGATTCC
 -223 CCATAGAATA TGAACCTCAA GGAGGTAAGC AAAGGGGTGT GTGGGATTCT TTGCTACTGG CTGCAGCTGC

FIG. 7 (CONTINUED)

-153 AGCCCCACCT CCTTCTCCAG CACATAAACA TTTCAGCAGC TTGACCTAAG ACTGCTGTGC AGGGCAGGGA
 -83 TGCTCCAGGC AGACAGGCCCA GCAAACAACA GCACACAGCT GAAAGTAAGA CTCAGAGGAG ACAGTTGAAG
 -13 AAGGCAAGTG GCGATG

Variant Sequences in the 5' flanking region of CYP3A5

Position	Variant sequence	Percentage
-1317	G-K (T or G) heterozygote	2.8% (1/36)
-988	T-Y (C or T) heterozygote	8.3% (3/36)
-657	C-Y (C or T) heterozygote	8.3% (3/36)
-475	T-K (T or G) heterozygote	30.6% (11/36)
-264	G-R (G or A) heterozygote	2.8% (1/36)
-147	A-R (A or G) heterozygote	30.6% (11/36)

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FIG. 8.

$$\begin{array}{cc} \begin{array}{c} + \\ + \end{array} & + \\ + & + \\ & \begin{array}{c} + \\ + \end{array} & + \\ + & + \\ & \begin{array}{c} + \\ + \end{array} & + \\ & + & + \\ & & + \end{array}$$

↓ shift

← free probe

1 2 3 4 5 6 7 8

FIG. 9.

```

      *           20           *           40           *           60
sites      : ----- :
HSCYPFLA_CYP3A6/7 : ----- :
HSRCYP3_CYP3A7    : ----- :
HSP4503A4_CYP3A4  : ----- :
S74699_CYP3A5     : ----- :
S74700_CYP3A5     : TAATAATTGGGTCGTTTATTTTAAATAATTAGCGTAAGTTGGGCGCTTTTAAAT : 60

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      *           80           *           100           *           120
sites : ----- :
HSCYPFLA_CYP3A6/7 : ----- :
HSRCYP3_CYP3A7 : ----- :
HSP4503A4_CYP3A4 : ----- :
S74699_CYP3A5 : ----- :
S74700_CYP3A5 : ATCTGAAA ATCTGAAATGGG TAT ATAGAT TGGGAT GGTC TGGGTATAT : 120

```

```

sites      :      *      140      *      160      *      180
HSCYPFLA_CYP3A6/7 : ----- :
HSRCYP3_CYP3A7    : ----- :
HSP4503A4_CYP3A4  : ----- :
S74699_CYP3A5     : ----- :
S74700_CYP3A5     : GGGAGAGAGGAGATATATATTGGTGGGATAT TGAGAGAATG ATATTT : 25
                  : GGGAGAGAGGAGATATATATTGGTGGGATAT TGAGAGAATG ATATTT : 32
                  : GGGAGAGAGGAGATATATATTGGTGGGATAT TGAGAGAATG ATATTT : 180

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sites      : -----*-----200-----*-----220-----*-----240-----
HSCYPFLA_CYP3A6/7 : -----[L1-RETROTRANSPOSON-ELEMENT]----- : 23
HSRCYP3_CYP3A7    : ----- : -
HSP4503A4_CYP3A4  : G T T G ----- G C T G A G G T -- G G T T G G G G T C C A T C T G G C T A T C ----- T G G G C : -
S74699_CYP3A5     : G T T T T T A C A A A T G C C A A G A T T T G G A A G C A A C C T A C A T G T C C A T C A A C A G A T G A A T G G G T : 64
S74700_CYP3A5     : G T T T T T A C A A A T G C C A A G A T T T G G A A G C A A C C T A C A T G T C C A T C A A C A G A T G A A T G G G T : 92
                  : G T T T T T A C A A A T G C C A A G A T T T G G A A G C A A C C T A C A T G T C C A T C A A C A G A T G A A T G G G T : 240

```

sites	*	260	*	280	*	300
HSCYPFLA_CYP3A6/7	:	-----		-----		-----
HSRCYP3_CYP3A7	:	-----		-----		-----
HSP4503A4_CYP3A4	:	A-----GCTGTTCTCTT		-----		-----
S74699_CYP3A5	:	AAAGAGAGTACTTCACTTATGCACAATGGAGTACAATTCAGCCATGAAAAAAGCATGAGA		-----		76
S74700_CYP3A5	:	AAAGAGAGTACTTCACTTATGCACAATGGAGTACAATTCAGCCATGAAAAAAGCATGAGA		-----		152
	:			-----		300

```

sites      : -----*-----320-----*-----340-----*-----360-----
HSCYPFLA_CYP3A6/7 : -----:-----
HSRCYP3_CYP3A7    : -----:-----
HSP4503A4_CYP3A4  : --CTCTCCTTTCT-----CTCCTGTTT-----:-----96
S74699_CYP3A5     : TCCTGTCTTTTATAATAATAACGTGGCTGGAAGTCAGGTCATTATGTTAGGTAAATAAG : 212
S74700_CYP3A5     : TCCTGTCTTTTATAATAG--CGTGGCTGGAAGTCAGGTCATTATGTTAGGTAAATAAG : 357

```

```

sites
HSCYPFLA_CYP3A6/7
HSRCYP3_CYP3A7
HSP4503A4_CYP3A4
S74699_CYP3A5
S74700_CYP3A5

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FIG. 9 (CONTINUED 1).

CYP3A4, CYP3A5, CYP3A6/7

sites	:	-----	440	-----	460	-----	480	:	-
HSCYPFLA_CYP3A6/7	:	-----		-----		-----		:	-
HSRCYP3_CYP3A7	:	-----		-----		-----		:	-
HSP4503A4_CYP3A4	:	-----		-----		-----		:	-
S74699_CYP3A5	:	-----		-----		-----		:	168
S74700_CYP3A5	:	-----		-----		-----		:	332
	:	-----		-----		-----		:	477
sites	:	-----	500	-----	520	-----	540	:	-
HSCYPFLA_CYP3A6/7	:	-----		-----		-----		:	-
HSRCYP3_CYP3A7	:	-----		-----		-----		:	-
HSP4503A4_CYP3A4	:	-----		-----		-----		:	-
S74699_CYP3A5	:	-----		-----		-----		:	207
S74700_CYP3A5	:	-----		-----		-----		:	391
	:	-----		-----		-----		:	537
sites	:	-----	560	-----	580	-----	600	:	-
HSCYPFLA_CYP3A6/7	:	-----		-----		-----		:	-
HSRCYP3_CYP3A7	:	-----		-----		-----		:	-
HSP4503A4_CYP3A4	:	-----		-----		-----		:	-
S74699_CYP3A5	:	-----		-----		-----		:	255
S74700_CYP3A5	:	-----		-----		-----		:	450
	:	-----		-----		-----		:	597
sites	:	-----	620	-----	640	-----	660	:	-
HSCYPFLA_CYP3A6/7	:	-----		-----		-----		:	-
HSRCYP3_CYP3A7	:	-----		-----		-----		:	-
HSP4503A4_CYP3A4	:	-----		-----		-----		:	-
S74699_CYP3A5	:	-----		-----		-----		:	303
S74700_CYP3A5	:	-----		-----		-----		:	508
	:	-----		-----		-----		:	656
sites	:	-----	680	-----	700	-----	720	:	-
HSCYPFLA_CYP3A6/7	:	-----		-----		-----		:	-
HSRCYP3_CYP3A7	:	-----		-----		-----		:	-
HSP4503A4_CYP3A4	:	-----		-----		-----		:	-
S74699_CYP3A5	:	-----		-----		-----		:	349
S74700_CYP3A5	:	-----		-----		-----		:	568
	:	-----		-----		-----		:	716
sites	:	-----	740	-----	760	-----	780	:	-
HSCYPFLA_CYP3A6/7	:	-----		-----		-----		:	-
HSRCYP3_CYP3A7	:	-----		-----		-----		:	-
HSP4503A4_CYP3A4	:	-----		-----		-----		:	-
S74699_CYP3A5	:	-----		-----		-----		:	391
S74700_CYP3A5	:	-----		-----		-----		:	628
	:	-----		-----		-----		:	776
sites	:	-----	800	-----	820	-----	840	:	-
HSCYPFLA_CYP3A6/7	:	-----		-----		-----		:	-
HSRCYP3_CYP3A7	:	-----		-----		-----		:	-
HSP4503A4_CYP3A4	:	-----		-----		-----		:	-
S74699_CYP3A5	:	-----		-----		-----		:	451
S74700_CYP3A5	:	-----		-----		-----		:	688
	:	-----		-----		-----		:	836

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FIG. 9 (CONTINUED 2)

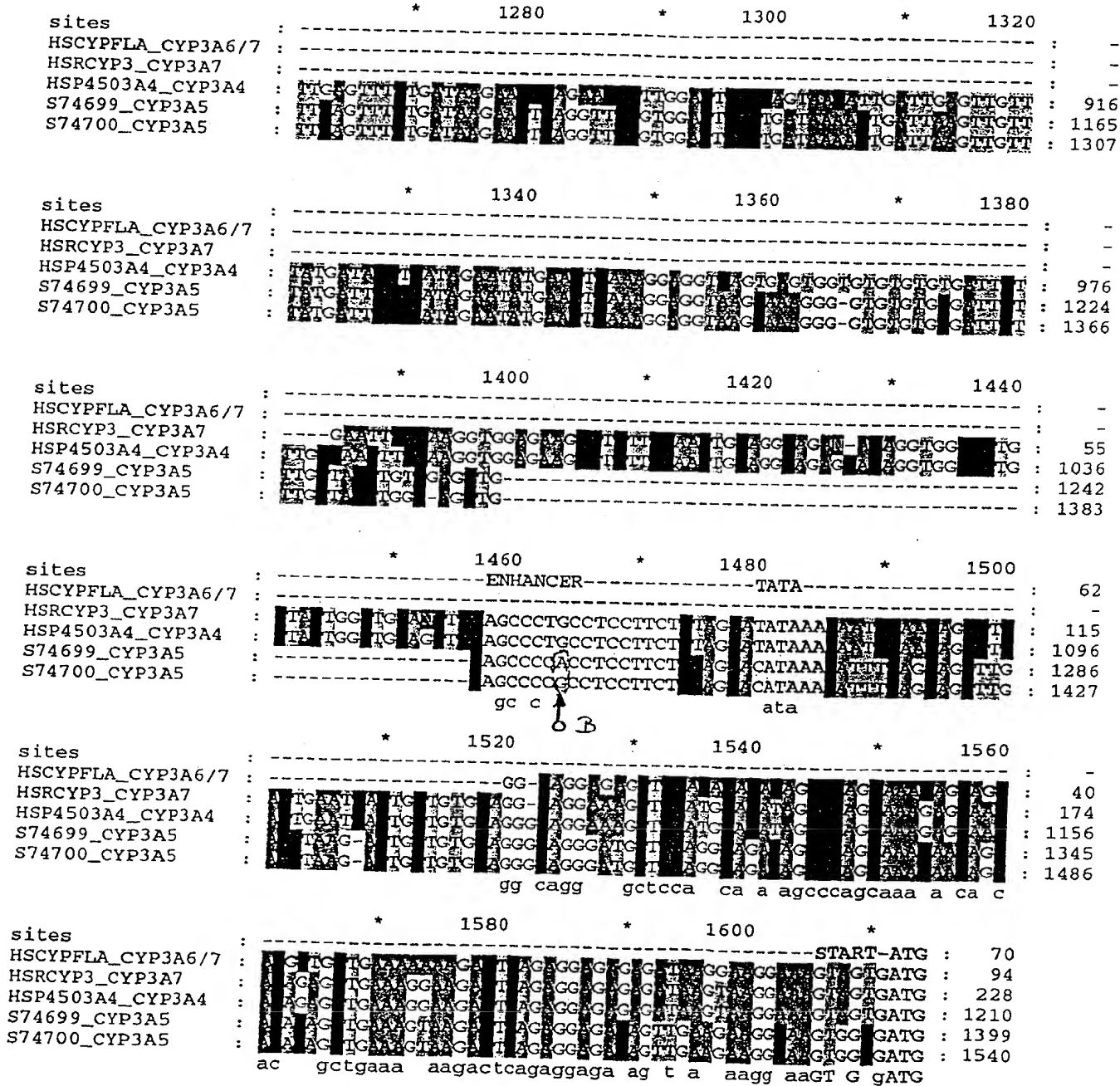
CYP3A4, CYP3A5, CYP3A6/7

		*	860	*	880	*	900	
sites	:	-----		-----		-----		:
HSCYPFLA_CYP3A6/7	:	-----		-----		-----		:
HSRCYP3_CYP3A7	:	-----		-----		-----		:
HSP4503A4_CYP3A4	:	-----		-----		-----		:
S74699_CYP3A5	:	-----		-----		-----		:
S74700_CYP3A5	:	-----		-----		-----		:
sites	:	*	920	*	940	*	960	:
HSCYPFLA_CYP3A6/7	:	-----		-----		-----		:
HSRCYP3_CYP3A7	:	-----		-----		-----		:
HSP4503A4_CYP3A4	:	-----		-----		-----		:
S74699_CYP3A5	:	-----		-----		-----		:
S74700_CYP3A5	:	-----		-----		-----		:
sites	:	*	980	*	1000	*	1020	:
HSCYPFLA_CYP3A6/7	:	-----		-----		-----		:
HSRCYP3_CYP3A7	:	-----		-----		-----		:
HSP4503A4_CYP3A4	:	-----		-----		-----		:
S74699_CYP3A5	:	-----		-----		-----		:
S74700_CYP3A5	:	-----		-----		-----		:
sites	:	*	1040	*	1060	*	1080	:
HSCYPFLA_CYP3A6/7	:	-----		-----		-----		:
HSRCYP3_CYP3A7	:	-----		-----		-----		:
HSP4503A4_CYP3A4	:	-----		-----		-----		:
S74699_CYP3A5	:	-----		-----		-----		:
S74700_CYP3A5	:	-----		-----		-----		:
sites	:	*	1100	*	1120	*	1140	:
HSCYPFLA_CYP3A6/7	:	-----		-----		-----		:
HSRCYP3_CYP3A7	:	-----		-----		-----		:
HSP4503A4_CYP3A4	:	-----		-----		-----		:
S74699_CYP3A5	:	-----		-----		-----		:
S74700_CYP3A5	:	-----		-----		-----		:
sites	:	*	1160	*	1180	*	1200	:
HSCYPFLA_CYP3A6/7	:	-----		-----		-----		:
HSRCYP3_CYP3A7	:	-----		-----		-----		:
HSP4503A4_CYP3A4	:	-----		-----		-----		:
S74699_CYP3A5	:	-----		-----		-----		:
S74700_CYP3A5	:	-----		-----		-----		:
sites	:	*	1220	*	1240	*	1260	:
HSCYPFLA_CYP3A6/7	:	-----		-----		-----		:
HSRCYP3_CYP3A7	:	-----		-----		-----		:
HSP4503A4_CYP3A4	:	-----		-----		-----		:
S74699_CYP3A5	:	-----		-----		-----		:
S74700_CYP3A5	:	-----		-----		-----		:

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FIG. 9 (CONTINUED 3).

CYP3A4, CYP3A5, CYP3A6/7



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FIG. 9(a).

```
A or G
=
MEME repeated motif 9
=====
MEME 'single' motif 9
=====
Yi-consensus
=====
apoE-undefined-site-3
=====
ApoE_B1
=====
APRT-human_US
=====
APRT-CHO_US
=====
1238 AGCTGCAGCCCCACCTCCTTCTCCAGC
      TCGACGTCGGGGTGGAGGAAGAGGTCG
.....
```

(B) A

FIG. 9(b).

```
MEME repeated motif 2
=====
MEME repeated motif 2
=====
MEME 'single' motif 9
=====
Yi-consensus
=====
Sp1-TPI_(4)
=====
GCF-consensus
=====
DSE_(1)
=====
IRE_(1)
=====
Sp1_CS4
=====
GC-box_(1)
=====
Sp1-IE-4/5
=====
Sp1-IE-3.3
=====
E2A_CS hsp70.2
=====
E2A_CSSp1-hsp70_(1)
=====
APRT-mouse_US
=====
1379 AGCTGCAGCCCCGCCTCCTTCTCCAGC
      TCGACGTCGGGGCGGAGGAAGAGGTCG
.....
```

(B) G

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FIG. 9(c).

```
MEME repeated motif 9
=====
MEME repeated motif 9
=====
MEME repeated motif 3
=====
MEME 'single' motif 6
=====
E-2.7_kb_(3)
=
E1A-F_CS
=====
GH1          MTVGRE_NRS
=====
910 TCTGTCTGGCTGGGCTTGCAAGGATGTGTAG (A)
    AGACAGACCGACCCGAACGTTCTCTACACATC T
.....
```

FIG. 9(d).

```
MEME repeated motif 9
=====
MEME repeated motif 9
=====
MEME repeated motif 9
=====
MEME repeated motif 3
=====
MEME 'single' motif 6
=====
E-2.7_kb_(3)
=
MBF-I_CS
=====
E1A-F_CS
=====
CNBP-SREMTVGRE_NRS
=====
GH1          MRE_CS2
=====
1052 TCTGTCTGGCTGGCGTGCAAGGATGTGTAG (A)
    AGACAGACCGACCGCACGTTCTCTACACATC G
.....
```